## REMARKS

It is respectfully requested that the above amendment be entered pursuant to the provisions of 37 C.F.R. §1.116(b); that this application be reconsidered in view of the above amendment and the following remarks; and that all of the claims remaining in this application be allowed.

Amendment

Applicants have requested that Claim 16 be amended to clarify that the claimed invention is directed to the treatment and prevention of congestive heart failure and not to endothelial disorders generically. In particular, Applicants have requested deletion of the phrase "medical disorders resulting from or involving endothelial dysfunction, wherein the disorder is selected from the group consisting of atherosclerosis, peripheral vascular disease . . . stroke, myocardial infarction, angina, hypertension, Raynaud's disease, cardiac syndrome X, migraine, ischemic damage, inflammatory bowel disease and graft versus host disease." Insofar as this amendment reduces claim scope without presenting any new claim language, no new issues are raised thereby. In addition, Applicants submit that this amendment places the claim in better condition for allowance or, alternatively, simplifies issues for Appeal and, accordingly, entry of the amendment is therefore proper. Applicants reserve the right to pursue the canceled subject matter in a continuation or divisional case.

Entry of this amendment is earnestly solicited.

These amendments have been made in accordance with 37 C.F.R. §1.121 as amended on November 7, 2000. As required, attached hereto in Appendix A is an illustration of the changes made to Claim 16.

Conformed Copy of the Pending Claims

Claims 16-28 are pending in this case. To facilitate review, attached hereto as Appendix B is a conformed copy of the pending claims wherein the amendments requested to Claim 16 have been presumed to have been entered.

Provisional Type Double Patenting Rejection

Claims 17-27 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 3-14 of copending Application No. 09/866,488 (hereinafter the '488 Application). This rejection is traversed for the following reasons.

Initially, Applicants maintain that a fair reading of this provisional rejection would suggest that this rejection is in fact over Claims 3-14 of the '488 Application ***in view of Henry, et al. (Pathobio., 67(5-6): 306-310 (1999)) (hereinafter "Henry") and further in view of Dini, et al., J. Cell. Sci., 108:967-973 (1995) ("Dini").*** The following comments have assumed that this is indeed the rejection made. If such an assumption is in error, the undersigned would appreciate clarification from the Office.

Secondly, Applicants note that an obviousness-type double patenting rejection is analogous to an obviousness rejection under 35 U.S.C. §103(a) except that application underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obvious-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. §103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991).

With regard to such determination, it is well established law that the test for non-obviousness articulated by the Court of Appeals for the Federal Circuit in *In re Vaeck* requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should practice the claimed methods; and (2) whether the prior art would also have provided a reasonable expectation of success to such a skilled artisan. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The first requirement goes to the question of motivation, and refers to a well established holding from earlier case law that there must be some logical reason at the time of the invention for modifying the reference or references along the lines of the invention; otherwise the use of the teachings as evidence of non-obviousness will entail prohibited hindsight. *Ex parte Stauber and Eberle*, 208 U.S.P.Q. 945, 946 (Bd. App. 1980).

The Office Action alleges that although the conflicting claims are not identical, they are not patently distinct from Claims 3-14 of the '488 application. Specifically, the Office Action states at page 2 that:

> "It is known in the art that the mechanism of action associated with the administration of apoptotic bodies is through the immune system's activation of inflammatory cells, such as macrophages or APC (see Henry *et al*). It is also known that apoptotic bodies are able ***to adhere to endothelial cell*** (as taught in light of Dini *et al* (J Cell Sci. 1995; 108:967-973)). (emphasis added)

Applicants disagree with this analysis and maintain that this rejection is in error because the combination of the claims in the '488 application and the two cited secondary references fails to provide for a *prima facie* case of obviousness against the claimed invention.

Specifically, the now claimed invention, as defined in Claim 16, is directed to methods for the treatment and/or prophylaxis of congestive heart failure.

Claims 17-28 in this application are all dependent claims and dependent claims include every limitation of the claim from which it depends. *See* MPEP §608.01(n). Thus the dependent claims are directed to the combination including everything recited in the independent claim and what is recited in the dependent claim and, accordingly, each of these dependent claims are directed to treatment of the same disease set as defined in Claim 16.

As to the '488 application, none of the claims in that application are directed to treatment and/or prophylaxis of CHF as recited in now presented Claims 16-28. Moreover, the final Office Action does not contend that the claims in the '488 application either teach or suggest the specific diseases treated by the methods of this invention. Accordingly, by themselves, the claims in the '488 application do not establish a *prima facie* case of obviousness against any of the claims of this application.

The cited Henry and Dini references fail to cure these deficiences. Henry, for example, does not disclose the treatment and/or prophylaxis of congestive heart failure. Rather, this reference is directed to the use of apoptotic bodies for treatment of cancer. *See,* Henry's Abstract. Likewise, Dini is directed to determine the role of the liver sinusoidal wall forming cells in the recognition mechanism of apoptotic bodies, and to

establish whether endothelial cells are also involved in this clearance.[1] Dini, however, does not disclose any therapeutic or prophylatic uses for such binding but merely is postulating such binding and the mechanism thereof.

In view of the above, neither Henry nor Dini teach or suggest congestive heart failure treated by the methods of this invention.

Since neither the claims of the '488 application, nor the teachings of either Henry or Dini teach or suggest congestive heart failure treated by the methods of this invention, the provisional rejection of Claims 17-27 under the judicially created doctrine of obviousness-type double patenting is in error.

Withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. § 102(b)

Claim 16 stands finally rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Henry. For the following reasons, Applicants submit that this rejection has been obviated.

The premise of this rejection is that the language of previously presented Claim 16 covered treatment of the specified medical conditions OR conditions involving endothelial disorders and that treatment of endothelial disorders such as cancers are disclosed by Henry. *See*, paragraph 5 at pages 3 and 4 of the final Office Action. Applicants disagree with this claim interpretation and submit that the prior claims were not directed to medical conditions generically involving endothelial disorders and, therefore, did not cover endothelial involved cancers. However, in order to expedite allowance of this application, Applicants have requested an amendment to Claim 16 which will delete any reference to endothelial disorders. Upon entry, Applicants submit that this rejection will be moot. Withdrawal of this rejection is requested.

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[1] See, for example, page 972, right column, first full paragraph of Dini, et al.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 17-19, 21 and 25-27 stand finally rejected under 35 U.S.C. § 103(a) as unpatentable over Henry. For the following reasons, Applicants submit that this rejection has been obviated.

As above, the premise of this rejection is that the language of previously presented Claim 16 covered treatment of the specified medical conditions OR conditions involving endothelial disorders and that treatment of endothelial disorders such as cancers are disclosed by Henry. *See*, paragraph 6 at pages 4 and 5 of the final Office Action. Applicants disagree with this claim interpretation and submit that the prior claims were not directed to medical conditions generically involving endothelial disorders and, therefore, did not cover endothelial involved cancers. However, in order to expedite allowance of this application, Applicants have requested an amendment to Claim 16 which will delete any reference to endothelial disorders. Upon entry, Applicants submit that this rejection will be moot. Withdrawal of this rejection is requested.

Withdrawn Rejections and Objection

Applicants note with appreciation that the prior rejections maintained under 35 U.S.C. §112, second paragraph, and under 35 U.S.C. §101 have been withdrawn.

Applicants also note with appreciation that the prior objection to Claim 15 has been withdrawn.

Co-pending Application/Publication

Applicants wish to bring the Examiner's attention to co-pending and allowed application 09/760,600, which is commonly assigned.

Applicants also wish to bring the Examiner's attention to PCT Publication No. WO 01/66785, published September 13, 2001.

Summary

In view of the above, Applicants submit that this application is in condition for allowance. A Notice to that effect is earnestly solicited.

Respectfully submitted,

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## APPENDIX A

## MARKED UP VERSION SHOWING CHANGES MADE TO THE AMENDED CLAM

Applicants have requested the following amendment to Claim 16:

-- 16. (Once amended.) A method for treatment and/or prophylaxis in mammalian patients with [medical disorders resulting from or involving endothelial dysfunction, wherein the disorder is selected from the group consisting of atherosclerosis, peripheral vascular disease,] congestive heart failure, [stroke, myocardial infarction, angina, hypertension, Raynaud's disease, cardiac syndrome X, migraine, ischemic damage, inflammatory bowel disease and graft versus host disease,] which method comprises administration to the patient of an effective amount of apoptotic bodies.--

## APPENDIX B

## CONFORMED COPY OF PENDING CLAIMS WITH AMENDMENT TO CLAIM 16 ENTERED

16. A method for treatment and/or prophylaxis in mammalian patients with congestive heart failure, which method comprises administration to the patient of an effective amount of apoptotic bodies.

17. The method of Claim 16 wherein the apoptotic bodies are in a liquid suspension along with viable cells.

18. The method of Claim 17 wherein the apoptotic bodies comprise from 10% to 90% of the cellular portion of the suspension.

19. The method of Claim 18 wherein the apoptotic bodies comprise from 30% to 70% of the cellular portion of the suspension.

20. The method of Claim 18 wherein the apoptotic bodies are derived from extracorporeal treatment of blood cells compatible with those of the mammalian patient.

21. The method of Claim 16 wherein the apoptotic bodies are derived from established cultured cell lines.

22. The method of Claim 20 wherein the blood cells are white blood cells of blood compatible with that of the mammalian patient.

23. The method of Claim 22 wherein the blood cells are the patient's own white blood cells.

24. The method of Claim 23 wherein the blood cells are the patient's own T lymphocytes.

25. The method of Claim 16 wherein the effective amount of apoptotic bodies comprises from 10,000 to 10,000,000 apoptotic bodies per kilogram body weight of the patient, administered as a dosage.

26. The method of Claim 25 wherein the dosage contains from 500,000 to 5,000,000 apoptotic bodies per kilogram body weight of the patient.

27. The method of Claim 25 wherein the dosage contains from 1,500,000 to 4,000,000 apoptotic bodies per kilogram body weight of the patient.

28. The method of Claim 25, wherein the mammalian patient is a human.